REMARKS

In the Claims:

Claims 22-26 are currently pending.

Applicants respectfully request that the Examiner consider the following remarks in response to the final Office action mailed 2/7/07. For the Examiner's convenience, Applicants note that as this Request for Reconsideration is submitted within 2-months of the mailing of the final Office action, an Advisory action is due if the claims are not found allowable.

Rejection under 35 U.S.C. § 101:

Claims 22-26 stand rejected under 35 U.S.C. § 101 for alleged lack of utility. In particular, the Office action alleges that "[t]he ability of the claimed protein to stimulate or inhibit lymphocyte proliferation in the MLR assay does not provide support for what specific conditions or for which specific diseases the claimed invention would predictably function for a therapeutic suppression of the immune system. Therefore, the results of the MLC or MLR assay in the instant specification are merely preliminary and do not support a specific and substantial utility for the claimed invention. Further . . . [t]here is insufficient data to conclude anything regarding the ability of an antibody that binds to the polypeptide PRO361 of the invention to be used in a substantial way to therapeutically inhibit an immune response, and much more experimentation would be required to use the invention in this manner." Pages 3-4 of the Office action mailed 2-7-07.

Applicants respectfully disagree. According to the Utility Guidelines, 66 Fed. Reg. 1092 (2001) ("Utility Guidelines"), a utility is "specific" when it is particular to the subject matter claimed. For example, it is generally not enough to state that a nucleic acid is useful as a diagnostic without also identifying the condition that is to be diagnosed. However, when the condition to be diagnosed is specifically identified, the asserted utility is "specific." The asserted utility for the claimed antibodies is specific because the

condition to be diagnosed or treated, suppression of immune response, is identified. More specifically, based on Example 34, found at page 141 of the specification, Applicants assert that the claimed antibodies, which bind PRO361, find specific utility in preventing suppression of an immune response.

Further, even though the "specific" utility of the present invention is diagnosing or treating suppression of an immune response, the law does not require that the claimed antibodies "predictably function for therapeutic suppression of the immune system" for that specific utility to be substantial. That is, a specific therapeutic use is not required for a substantial utility. Rather, a substantial utility may be simply based on *in vitro* test results that provide evidence of a pharmacological activity. The requirement of "substantial utility" defines a "real world" use, and derives from the Supreme Court's holding in *Brenner v. Manson,* 383 U.S. 519, 534 (1966) stating that "[t]he basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility." Section 2107.01 of the MPEP cautions, however, that Office personnel must be careful not to interpret the phrase "immediate benefit to the public" or similar formulations used in certain court decisions to mean that products or services based on the claimed invention must be "currently available" to the public in order to satisfy the utility requirement. "Rather, **any reasonable use that an applicant has identified for the invention that can be viewed as providing a public benefit should be accepted as sufficient,** at least with regard to defining a "'substantial'" utility.'" *See* MPEP § 2107.01 (emphasis added). Indeed, the Guidelines for Examination of Application for Compliance with the Utility Requirement, set forth in MPEP § 2107 II(B)(I) gives the following instruction to patent examiners: "If the applicant has asserted that the claimed invention is useful for any particular practical purpose . . . and the assertion would be considered credible by a person of ordinary skill in the art, do not impose a rejection based on lack of utility." Here Applicants have asserted that the claimed invention is useful for a practical purpose, *i.e.* suppression of an immune response.

One case discussed in the MPEP involves facts similar to those present in this case. Specifically, in discussing the requirements of a "substantial utility," Section 2107.01 of

the MPEP refers to *Nelson v. Bowler,* 626 F.2d 853 (CCPA 1980) where the court reversed a finding by the Office that the applicant had not set forth a "practical" utility under 35 USC § 101. In *Nelson,* two experiments were relied on to provide utility, a rat blood pressure test (BP) and a gerbil colon smooth muscle test (GC-SMS). The *Nelson* inventors were using these tests on novel compounds and comparing the results to natural control prostaglandins PGF alpha and PGE1. In the BP test, the blood pressure of anesthetized rats was recorded by polygraph to determine if a novel compound would have a lowering or elevating effect on blood pressure when compared with PGE1. Two novel compounds tested positive in this test, and at trial, testimony was given on the reliability of the BP test, with a scientist stating that it had been in use between five and six years and had produced excellent results. The GC-SMS test was an *in vitro* test comprising excising a section of colon from a gerbil, and connecting a lever arm that would measure the contraction of the smooth muscle in response to a novel compound. Again, a naturally occurring PGE was used as a positive control. The same novel compounds that tested positive in the rat BP assay also tested positive in the GC-SMS test. The USPTO Board of Interferences and Patent Appeals characterized these tests as "rough screens, uncorrelated with actual utility" and rejected the utility based on these tests. **The court found the Board erred in not recognizing that tests providing evidence of a pharmacological activity yield a practical utility even though they may not establish a specific therapeutic use**. The court held that "knowledge of the pharmacological activity of any compound is obviously beneficial to the public" and "since it is crucial to provide researchers with an incentive to disclose pharmacological activities in as many compounds as possible, we conclude that adequate proof of any such activity constitutes a showing of practical utility."

In the present case, Applicants rely on the *in vitro* MLR assay to demonstrate that the claimed invention has pharmacological activity, *i.e.* suppression of an immune response. The legal standard with respect to *in vitro* or animal model data providing pharmacological activity has been commented on in *Cross v. Iizuka,* 753 F.2d 1040, 1051 (Fed. Cir. 1986) The assay used in *Cross* was a platelet microsome assay, consisting of an *in vitro* milieu consisting of blood platelets and other finely granular elements of protoplasm, such as ribosomes, fragmented endoplasmic reticula and

mitochondrial cristae. In *Cross,* the Federal Circuit found an *in vitro* assay, the inhibition of thromboxane synthetase in human or bovine platelet microsomes, satisfied the utility requirement:

> "We perceive no insurmountable difficulty, under appropriate circumstances, in finding that the first link in the screening chain, *in vitro* testing, may establish a practical utility for the compound in question. **Successful *in vitro* testing will marshal resources and direct the expenditure of effort to further *in vivo* testing of the most potent compounds, thereby providing an immediate benefit to the public, analogous to the benefit provided by the showing of an *in vivo* utility."**

Cross v. Izuka, 753 F.3d at 1051 (Emphasis added). Thus, Applicants respectfully submit that the results of the *in vitro* MLR assay adequately support the asserted utility for the claimed invention.

Moreover, no case, rule, or statute **requires** explicit data values to support an applicant's assertion of utility. Rather, "[p]roof of utility is sufficient if it is convincing to one of ordinary skill in the art." *In re Jolles,* 628 F.2d 1322 (CCPA 1980) citing *In re Irons,* 340 F.2d 974 (CCPA 1965). Indeed, "[t]he amount of evidence required depends on the facts of each individual case . . . the character and amount of evidence needed may vary, depending on whether the alleged utility appears to accord with or contravene established scientific principles." *In re Jolles,* 628 F.2d 1322 (CCPA 1980) (citations omitted). That is - more definite and stronger evidence of utility is required when an asserted utility appears to contravene established scientific principles. In contrast, less evidence is required when an asserted utility accords with established scientific principles. Put another way, an applicant's assertion of utility in a patent specification "must be taken as sufficient to satisfy the utility requirement of § 101 for the entire claimed subject matter unless there is a reason for one skilled in the art to question the objective truth of the statement of utility or its scope." *In re Langer,* 503 F.2d 1380, 1391 (CCPA 1965) (emphasis original). Thus, Office personnel are directed to presume that a statement of utility by an applicant is true. To overcome the presumption of truth that an assertion of utility by an applicant enjoys, Office personnel must establish that it is more likely than not that one of ordinary skill in the art would doubt (*i.e.* "question")

the truth of the statement of utility. According to § 2107.02 of the MPEP, "[t]o do this, Office personnel must provide evidence sufficient to show that the statement of asserted utility would be considered 'false' by a person of ordinary skill in the art."

In the present case there is no evidence that the asserted utility of antibodies that bind PRO361, based on the immunosuppressive activity of PRO361 shown in the MLR assay, would be considered 'false' by a person of ordinary skill in the art. Previously, the Office provided evidence that it argued indicated that one of ordinary skill in the art would not accept the MLR assay as a means of identifying immunosuppressive agents. However, that evidence has been overcome and the Office has acknowledged that "[t]he art does recognize that the MLR assay is useful in screening a compound that could have a rule in immune response." Page 3 of the Office action mailed 2/7/07. Therefore, clearly Applicants' assertion of utility, which is based on the activity of PRO361 observed in the MLR assay, does not contravene any scientific principles but rather accords with them. Thus, Applicants assertion of utility should be accepted.

Indeed, "any reasonable use that an applicant has identified for the invention that can be viewed as providing a public benefit should be accepted as sufficient." MPEP § 2107.01. The Guidelines for Examination of Applications for Compliance with the Utility Requirement, set forth in MPEP § 2107 II (B) (1) gives the following instruction to patent examiners: "If the applicant has asserted that the claimed invention is useful for any particular practical purpose . . . and the assertion would be considered credible by a person of ordinary skill in the art, do not impose a rejection based on lack of utility." The Utility Guidelines restate the Patent Office's long established position that any asserted utility has to be "credible." "Credibility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure and any other evidence of record . . . that is probative of the applicant's assertions." MPEP § 2107 II (B) (I) (ii). Such a standard is presumptively satisfied unless the logic underlying the assertion is seriously flawed, or if the facts upon which the assertion is based are inconsistent with the logic underlying the assertion. (Revised Interim Utility Guidelines Training Materials, 1999).

According to these standards, Applicants have clearly satisfied the utility requirement. First, as stated above, the Office has recognized that the MLR assay is art-recognized

and accepted for identifying molecules that suppress an immune response. Second, in addition to explaining how to conduct the MLR assay, Example 34 of the present specification, through reference to the *Current Protocols in Immunology,* also explains how to calculate the results obtained from the MLR assay. One of ordinary skill in the art could easily carry out the MLR assay as described in the specification and *Current Protocols,* and calculate the results as taught by the specification and *Current Protocols.* Applicants have provided sufficient detail in the specification, either explicitly or through incorporation by reference, about the MLR assay, how the assay is performed, what controls are used and how they are used, and how the data is calculated. Third, Applicants' assertion of utility based activity observed in the MLR assay clearly is neither seriously flawed, nor are the facts upon which the assertion is based inconsistent with the logic underlying the assertion. Specifically, at page 141 of the specification, Applicants assert that PRO361 exhibited a significant inhibitory effect in the MLR assay. That assertion is based upon the fact that PRO361 "tested positive" in the MLR assay. According to the specification the standard for identifying immunosuppressive molecules using the MLR assay is as follows: "[a]ny decreases below control is considered to be a positive result for an inhibitory compound, with decreases of less than or equal to 80% being preferred. However, any value less than control indicates an inhibitory effect for the test protein."

This standard is art recognized. For example, the Declaration of Sherman Fong, Ph.D., previously submitted by Applicants with the Amendment and Response mailed August 3, 2005, provides evidence that one of at least ordinary skill in the art accepts this standard. Specifically, as illustrated by his *Curriculum Vitae* attached to his Declaration, Dr. Fong is someone of at least ordinary skill in the art. In his opinion, Dr. Fong attests that "[i]t is my considered scientific opinion that a PRO polypeptide shown to inhibit T-cell proliferation in the MLR assay where the activity is observed as 80% or less of the control, as specified in the present application, would be expected to find practical utility when an inhibition of the immune response is desired, such as in autoimmune diseases." Clearly then, Dr. Fong does not find that the utility of PRO361 alleged at page 141 of the specification contravenes any established scientific principles, but rather attests that the alleged utility accords with them.

Indeed, Dr. Fong is the inventor on another patent application that has been allowed since Applicants' last response, which was submitted November 8, 2006. Specifically, U.S. Patent Application Serial No. 10/213,181 was allowed 1/10/07 and the issue fee was paid 3/5/07. Significantly, this patent sets forth the *same* standard for assessing immunosuppressive ability of a test protein as is set forth in the present application. Specifically, at paragraph 388, the specification of U.S. Patent Application Serial No. 10/213,181 reads:

> Any decreases below control is considered to be a positive result for an inhibitor compound, with decreases of less than or equal to 80% being preferred. However, ***any value less than control indicates an inhibitory effect*** for the test protein.

Emphasis added. In contrast to the present application, specific data values for the percent decrease observed in the MLR assay are provided in the specification of the above-identified patent. However, it is significant that the values corresponding to the claimed protein range from an ***18% decrease below control to a 75% decrease below control***. Thus, this evidence further supports Applicants' assertion that *any* decrease below control indicates an inhibitory effect for the test protein. *See also* US Patent No. 5,958,403 at col. 6, ll 16-19, which states that "[u]seful constructs are also those which provide a mixed lymphocyte reaction (MLR) by decreasing proliferation by 20%, more preferably 40%, and most preferably by 60% relative to control cells." These references provide clear evidence that it is improper to require an explicit demonstration that a test compound exhibits at least an 80% decrease compared to control, a level that is explicitly characterized as being ***preferred not necessary*** in the present specification. This evidence also provides further support for Applicants assertion that one of ordinary skill in the art would not doubt Applicants' assertion of utility based on PRO361 testing positive in the MLR assay.

The specification clearly states that PRO361 tested positive in the MLR assay. Therefore, although no explicit data is provided, in light of the significant details provided about the MLR assay, how it was performed, what controls were used, how they were used, how the positive result was determined, the art recognition of the MLR

assay as a means of identifying immunosuppressive compounds, and the testimony of Sherman Fong presented in the Fong Declaration, one of ordinary skill in the art can conclude that PRO361 exhibited a level of inhibition greater than any inhibition seen with the controls and can conclude that PRO361 has immunosuppressant characteristics. Therefore, antibodies that bind PRO361 will find utility in preventing suppression of the immune system, for example in cancer and HIV treatments.

Indeed, in view of these significant teachings and the high level of skill and understanding in the art, the lack of explicit data does not make it more likely than not that one of ordinary skill in the art would doubt Applicants' assertion of utility for the PRO361 polypeptide. This is sufficient to satisfy the utility requirement. As stated in *Nelson v. Bowler,* 626 F.2d 853, 206 USPQ (BNA) 881 (C.C.P.A. 1980), tests evidencing pharmacological activity of a compound establish practical utility, even though they may not establish a specific therapeutic use. Moreover, while Applicants have provided the Fong Declaration, which clearly states that one of at least ordinary skill in the art does not find the asserted utility to violate or contravene any established scientific principles, US Patent No. 5,958,403, and allowed US Patent Application Serial No. 10/213,186, which both evidence that the standard set forth in the present application is art-recognized and accepted, the Office has not provided any evidence showing that the asserted utility would be considered "false" by a person of skill in the art. Therefore, Applicants have provided sufficient proof of utility for claims 22-26 and respectfully request that this ground of rejection be withdrawn.

Rejection under 35 U.S.C. § 112, first paragraph:

Enablement

Claims 22-26 also stand rejected under 35 U.S.C. § 112, first paragraph because allegedly one of ordinary skill in the art would not know how to make and use the claimed invention because allegedly the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

Applicants respectfully disagree. As discussed above, the claimed antibody has the specific, substantial, and credible utility of binding a polypeptide that inhibits the

proliferation of stimulated T-lymphocytes as demonstrated in the MLR assay experiment discussed in Example 34 at page 141 of the application. Applicants respectfully request the Examiner reconsider and withdraw the rejection of the claims under 35 U.S.C. § 112 ¶1 for alleged inadequate disclosure on how to use the claimed invention.

CONCLUSION

Applicants believe this Request for Reconsideration fully responds to the final Office action mailed February 7, 2007. Applicants respectfully request the Examiner grant allowance of pending claims 22-26. The Examiner is invited to contact the undersigned attorney for the Applicant via telephone if such communication would expedite allowance of this application.

Respectfully submitted,

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